Resistant Urinary Tract Infections

Combined Autogenous Vaccine and Drug Therapy

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• **The "miracle" antibiotics and sulfa drugs have been found unsatisfactory in treating certain severe resistant urinary tract infections apparently due to lack of immunity factor in the patient. Of a series of 56 patients with resistant urinary tract infection who were treated with autogenous vaccine and then with sulfa drugs, 26 were completely cured.**

ADEQUATE IMMUNITY FACTORS bear important relationship to the effectiveness of drug therapy in urinary tract infections, for they can be synergistic with drugs in relief of disease.

Host resistance (immunity) to infection is of two main types—acquired and natural. *Acquired immunity* follows external influence and is due to presence of antibodies. *Natural immunity* is an inherent individually variable constitutional property of man and animals.

The importance of the host's resistance or immunity to infection has received scant attention by urologists in recent years, owing to the immediate dramatic responses to chemotherapeutic agents and antibiotics in many cases. Now the need for attention to improvement of a patient's immunity is becoming more important for several reasons: The increasing number of drug-resistant bacteria, toxic effects of antibiotics, the large numbers of superinfections, and allergic sensitivity to drugs.

Meyer[3] in 1938 demonstrated the ineffectiveness of chemotherapy without the presence of adequate numbers of antibodies. In experiments that he reported, vaccinated mice treated with sulfapyridine survived an otherwise lethal streptococcic peritonitis. A high opsonic index was noted in animals receiving such combined treatment whereas control animals, either vaccinated or treated with sulfapyridine alone, all died and had minimal phagocytosis of streptococci in the peritoneal exudate.

Hence the author made a study of a method of treatment combining drug therapy with measures to enhance immunity in cases of drug-resistant urinary tract infection. Patients who previously had been treated with all appropriate drugs and combinations, without effect, were considered for "combined therapy," which consisted of (1) stimulating immunity with autogenous vaccines, stock vaccines or gamma globulin for "priming" of host resistance, followed by (2) drug therapy with sulfonamides, administration of antibiotics orally or parenterally, and urethral instillations of neomycin, bacitracin or polymyxin or combinations of these.

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The present report will deal with results obtained in 56 cases in which combined autogenous vaccine and sulfonamide therapy was used. Autogenous vaccine was made with from one to three kinds of organisms found in the urinary tract of the patient.

Autogenous vaccine, 0.1 cc. weekly, was given intradermally in 25 cases and subcutaneously in 31 cases. Sulfadiazine and triple sulfa combinations were used in most cases. Sulfisomidine, sulfisoxazole and sulfamethylthiadiazole were also used. Since the series was small no attempt was made to correlate the results with the various sulfonamides used.

Of the 56 patients, 23 were bacteriologically and clinically cured and 33 had persistent pyuria (Table 1). Three of the 33 were finally able, however, to undergo corrective operation with resultant cure of pyuria; and it was of interest in those cases that the postoperative course was extremely smooth in spite of operation in a field definitely infected by antibiotic-resistant organisms. It was conjectured that the vaccine might have had some influence.

Methenamine mandelate had no effect either before or after the vaccine was given in any of the patients. Nitrofurantoin N.N.R. was given to some of the patients after the therapy described gave no benefit, but it had no effect.

Redewill,[5] in a paper on antibiotic combinations which he presented in 1952 before the Western Section of the American Urological Association, discussed a related subject, just at the time when the earlier patients in the present series were being treated. Redewill described a unique method of producing a more specific gamma globulin by using donors previously vaccinated against resistant bacteria common in urinary tract infections. It is of note in this regard that one patient in the present series with long-standing infection of the urinary tract, who had been treated unsuccessfully with combined

TABLE 1.—*Results of therapy of resistant urinary tract infection with autogenous vaccine and sulfa drugs*

Disease	Total Number	Cure	Failures
Recurrent cystitis and urethritis	17	9	8
Prostatitis, urethritis, with urethral strictures well dilated	19	8	11
Chronic pyelonephritis (Postparathyroid-adenectomy, calculi, 1 case); (Postoperative Staghorn calculi, 1 case); (Severe Friedlander's bacilluria, 1 case)	8	3	5
Diffuse leukoplakia of bladder	1	....	1
Empyema and calculus in stump of ureter	2	....	2
Multiple urethral diverticuli	1	....	1
Stricture after radical perineal prostatectomy	1	1	....
Postirradiation cystitis	1	....	1
Persistent postprostatectomy pyuria (all with trabeculation and cellules)	6	2	4
	56	23	33

autogenous vaccine and sulfa drugs, brought two large ampules of gamma globulin to the author with the request that they be given to him. He had been exposed to poliomyelitis, he explained, and the ampules of gamma globulin had been given to him by the health department. The patient was receiving sulfonamides for pyuria at the time. The gamma globulin was injected and a week later the urine was free of pathogenic organisms for the first time in two years. It seems probable that the antibodies or natural immune factors present in the gamma globulin were responsible for the cure. Whether the sulfonamide action was enhanced by synergism is a matter of conjecture.

DISCUSSION

Synergism between specific antibodies and sulfonamides has been suggested in other reports. Cokkinis and McElligott[1] suggested that sulfonamides in treating gonorrhea were most effective in patients who had had the disease long enough to acquire some immunity. Some observers believe the mode of sulfonamide action is to render the organisms more susceptible to the host's antibodies (Meyer[3]). Until more is known regarding the bacteriostatic action of antibodies, sulfonamides and antibiotics, this mechanism cannot be conclusively interpreted.

The future may bring combined mixed stock vaccines which will be long-acting after a single injection. Further studies of gamma globulin and properdin may make specific injectables available.

Urologically, the immune factor may be valuable, with the evidence pointing to lack of excretion of antibiotics by the prostate gland (Pulaski[4]).

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